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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,699	03/30/2001	Munehide Kano	50026/022002	7451

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	
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06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/823,699	KANO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,5,7,9,11-20,24,26,28-33,37,39,42-45,62-68,70 and 73-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,5,7,9,11-20,24,26,28-33,37,39,42-45,62-68,70 and 73-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 3/19/2007 are acknowledged. Claims 41, 69, 71, 72 have been canceled. Claims 2, 5, 12, 16, 17, 28, 33, 42, 67, 68, 70 have been amended. Claims 73-79 are newly submitted. Claims 2, 4, 5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 42-45, 62-68, 70, 73-79 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 3/19/07 response would be addressed to the extent that they apply to current rejection.

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of Claims 67-71 under 35 U.S.C. 112 first paragraph, is withdrawn in view of claim amendment.

The prior rejection of Claims 20, 24, 26, 28, 30-33, 37, 39, 41, 43-45, 63-72 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the newly submitted evidence.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 4, 16-19, 65, 66 stand rejected under 35 U.S.C. 103(a) as being obvious over *Nagai et al* (US 7,101,685), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52), and as evidenced by *Henke et al* (Vaccine 1999;17:589-96) for reasons of record and following.

Applicant argues that even if Sendai virus was successfully used to express an immunodeficiency viral protein, there is no reasonable expectation of success for using Sendai virus in place of vaccinia virus used as a vaccine as taught by Hirsch et al because Sendai virus is a negative-strand RNA virus and Vaccinia virus is a DNA virus, they act differently in cells.

In response, as an initial matter, the instantly rejected claims are drawn to a composition having the structure of a Sendai virus encoding an immunodeficiency viral protein, and the prior art are applied based on the structure of the composition, not the intended use of the composition. This is because the use of a product for a particular

purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand-alone. The MPEP states, "IN APPARATUS, ARTICLE, AND COMPOSITION CLAIMS, INTENDED USE MUST RESULT IN A STRUCTURAL DIFFERENCE BETWEEN THE CLAIMED INVENTION AND THE PRIOR ART IN ORDER TO PATENTABLY DISTINGUISH THE CLAIMED INVENTION FROM THE PRIOR ART." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). As discussed previously, according to the combined teachings, it is apparent that it was well within the levels of the skilled to make such a construct and be reasonably successful to express the S/HIV protein in mammalian cells.

Further, even when considering the intended use, at the time of instant filing date, it was well known in the art that many virus vectors have made available in the gene therapy art, each has its own characteristics. It was quite common for the skilled in the art to use various vectors interchangeably to carry a transgene taking advantage of a particular characteristic of the viral vector for a specific need in gene therapy, such as host cell range, capability of replication in non-dividing cells, and tissue tropism. In the case of genetic vaccination, whether the vector is a DNA virus or RNA virus, it was used to sufficiently express an antigen in a host cell to stimulate the host immune response specific to such antigen, thus as long as the viral vector could sufficiently express the antigen at high enough levels in the host cells, there is a reasonable expectation of success in inducing an immune response regardless the mechanism how the antigen was produced in the host cell. Here, *Yu et al* have sufficiently established that V gene

defective Sendai viral vector could efficiently express an HIV viral antigenic protein at a level comparable to a vaccinia viral vector, (which implicitly suggested the intention of using the Sendai viral vector in place of an vaccinia vector); and *Hirsch et al* have established it is efficient to use a recombinant vaccinia viral vector to express HIV gag-pol proteins in Macaques and obtaining protective effects. Thus the skilled artisan would have had a reasonable expectation of success to express SHIV proteins in a subject with a recombinant sendai virus vector in place of a vaccinia vector since they express HIV protein in comparable levels. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Applicant then argues that *Hanke et al* neither suggests nor motivates the skilled worker to arrive at the claimed inventions.

In response, *Hanke et al* was relied on to establish it would have been obvious for the skilled artisan to make a vector construct for expressing either a full-length protein or an *epitope* thereof for developing a genetic AIDS vaccine. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 2, 4, 5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 42-45, 62-66, 68, 70, 73, 75, 76 stand or newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), *Seth et al* (PNAS 1998;95:10112), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hurwitz et al* (Vaccine 1997;15:533-40); and as evidenced by *Ourmanov et al* (J Virol 2000;74:2740-51, IDS), *Hanke et al* (Vaccine

1999;17:586-96), and *Nakanishi et al* (J Controlled Release 1998;54:61-8), for reasons of record and following.

Flanagan et al teach using a recombinant adenovirus expressing SIV Gag protein for vaccination in mice by intranasal inoculation, and teach that mucosal route of delivery is desirable for inducing a cellular immune response. *Seth et al* teach administering a recombinant vaccinia virus vector expressing gag-pol fusion polypeptides in multiple dosages (day 1 and 126) and inducing cytotoxic immune response specific to gag pol proteins in a rhesus monkey. *Ourmanov et al* evidenced that VV-gag-pol vaccine (as used by *Seth et al*) indeed provided protection from high levels of viremia and AIDS following challenge with a pathogenic strain of SIV in macaques.

Claims 68, 70 are drawn to a part of an immunodeficiency viral protein that is an epitope. *Seth et al* teach that cytotoxic T lymphocytes are important in containing the spread of HIV-1 in infected individuals, and the induction of a specific CTL response generally requires just a short peptide (epitope) in association with a MHC class I molecule (e.g. column 1, page 10112). Although not relied upon, *Hanke et al* have shown using multi-epitope strategy for inducing HIV-specific CTL for vaccination.

The teachings of *Flanagan et al* and *Seth et* al established the state of the art in developing genetic vaccines for AIDS, although they did not teach a particular vector, sendai viral vectors, *Yu et al* cured the deficiency. *Yu et al* supplemented the teaching of *Flanagan et al* and *Seth et al* by establishing the advantage of using sendai virus, particularly V(-) sendai virus as a expression vector in expressing a HIV protein, and its expression efficiency in cells that are natural hosts for AIDS virus. *Yu et al* teach the need for establishing a better system to express HIV antigen in natural host cells for HIV such as human primary blood mononuclear cells, macrophages or T cells (e.g. abstract), and compared the V- SeV with the commonly used *vaccinia virus vector* that was used by *Seth*, and teach "THE V(-) VERSION APPEARS TO BE EXCELLENT AND ALMOST COMPARABLE TO THE ABOUVE NOTED VV-BASED EXPRESSION" (column 1, page 462, emphasis added). Clearly, *Yu et al* teach that sendai virus could be used as a gene transfer vector

for expressing a nonanalogous viral protein, such as the immunodeficiency virus protein, in place of the vaccinia virus or interchangeably with other known viral vectors. *Yu et al* further teach the advantages of a V(-)SeV such as a robust heterologous gene expression capability in mammalian cells, moderate pathogenesis, and broad host range.

Hurwitz et al supplemented the combined teaching by establishing the feasibility of sendai virus nasal inoculation. *Hurwitz et al* teach nasal inoculation of sendai virus is non-pathogenic for primates. *Hurwitz et al* also teach the effectiveness of intranasal multiple inoculation (abstract, figures 1-4, and table 1). *Hurwitz et al* go on to teach the advantage of using Sendai virus as a potential human vaccine because its long-lasting effect stimulating memory B-cells as well as CTL response (last paragraph, page 539).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* or *Seth et al*, by substituting and/or combining the recombinant adenoviral or vaccinia vector with a Sendai viral vector as taught by *Yu et al*, for expressing an immunodeficiency virus protein or an epitope thereof, and delivering such via intranasal inoculation as taught by *Flanagan* et al, and *Hurwitz et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention given the knowledge that the V(-) sendai virus vector could efficiently expressing an HIV antigenic protein in natural host cells for immunodeficiency virus, and given numerous carrier vectors known and used in the art, and all proven to be effective in expressing a viral protein at sufficient levels. Thus, the limitation falls within the bound of optimization for the skilled artisan to determine which vector would serve their goal the best.

New claims are drawn to the immunodeficiency viral protein in the form of a protease-processed protein. Applicant pointed to page 22 of the specification, which cited prior art to teach various protease cleaved fragments of SHIV proteins. Thus, the knowledge was well known in the art at the time of the instant priority date. This could

be seen in the teaching of *Yu et al*, who teach gp120 is the extracellular subunit of the gp160 derived via proteolytic processing (e.g. the 1st paragraph of page 457).

Applicant argues that *Flanagan et al* teach an adenoviral vector and *Hirsch et al* teach a vaccinia vector; they both are DNA vectors while Sendai virus is a negative-strand RNA virus, they act differently in cells. This argument has been addressed *supra*, will not reiterate here.

As to the gene transfer or gene expression vectors, the applicant alleges the Office has not considered all the limitations of the claims as to the "gene-transfer".

In response, the Office has indeed considered the limitation (e.g. see page 13 of the Office action mailed 9/14/06) and concluded in the absence of a clear distinction, and in view of the common knowledge in the art, the vectors in the cited art are considered to meet claim limitation because the specification fails to specifically teach how gene-transfer vector differs from gene expression vector structurally. Both *Yu et al* and *Seth et al* are published before instant priority date, and illustrated the state of the art with regard to using expression vectors for gene transfer.

Applicant then argue it would not have been obvious as to whether a recombinant Sendai virus persists in the nasal cavity for several days as found for wild-type virus as taught by *Hurwitz et al.*

In response, this limitation of "persists for several days" is not in any of the claims. Even if it will be, one can always apply multiple doses as taught by the combined references.

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claims 78, 79 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), *Seth et al* (PNAS 1998;95:10112), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hurwitz et al* (Vaccine 1997;15:533-40) as applied to claims 2, 4, 5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 42-45, 62-66, 68, 70, 73, 75, 76 above, and further in view of *Göttlinger et al* (PNAS 1989;86:5781-5).

Although the combined teachings of *Flanagan et al*, *Seth et al*, in view of *Yu et al*, and *Hurwitz et al* do not particularly teach the particular proteins as recited in these claims, they were known in the art, not the discovery of the applicant.

It would have been obvious for the skilled in the art to use the Sendai viral vector to exploit the SHIV protein derivatives in search for an effective antigenic epitope with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 11-13, 15, 74 stand or newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS), for reasons of record and *supra*.

Claim 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997

Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, 15, 74 above, further in view of *Boutillon et al* (US 6,015,564), for reasons of record and *supra*.

Claim 67 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, 15, 74 above, further in view of *Hanke et al* (Vaccine 1999;17:589-96), for reasons of record and *supra*.

Claim 77 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, 15, 74 above, further in view of *Göttlinger et al* (PNAS 1989;86:5781-5).

Although the combined teachings of *Flanagan et al*, in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* do not particularly teach the particular proteins as recited in claim 77, they were known in the art, not the discovery of the applicant.

It would have been obvious for the skilled in the art to exploit the protein derivatives in search for an effective antigenic epitope with a reasonable expectation of success. Thus, the claimed invention as a whole was prima facie obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 4, 16-19, 65, 66, 69, 75 stand or newly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 13 of copending Application No. 09/728,207, now U.S. patent 7,101,685, in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), *Hirsch et al* (J Virol 1996;3741-52), and *Hanke et al* (Vaccine 1999;17:589-96) for reasons of record and *supra*.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
June 7, 2007